TOXCAST ASSAY DESCRIPTIONS

Development of Context-Rich Test Method Descriptions for High-throughput Toxicity Studies

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Disclaimer: *The views expressed in this poster are those of the authors and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.*

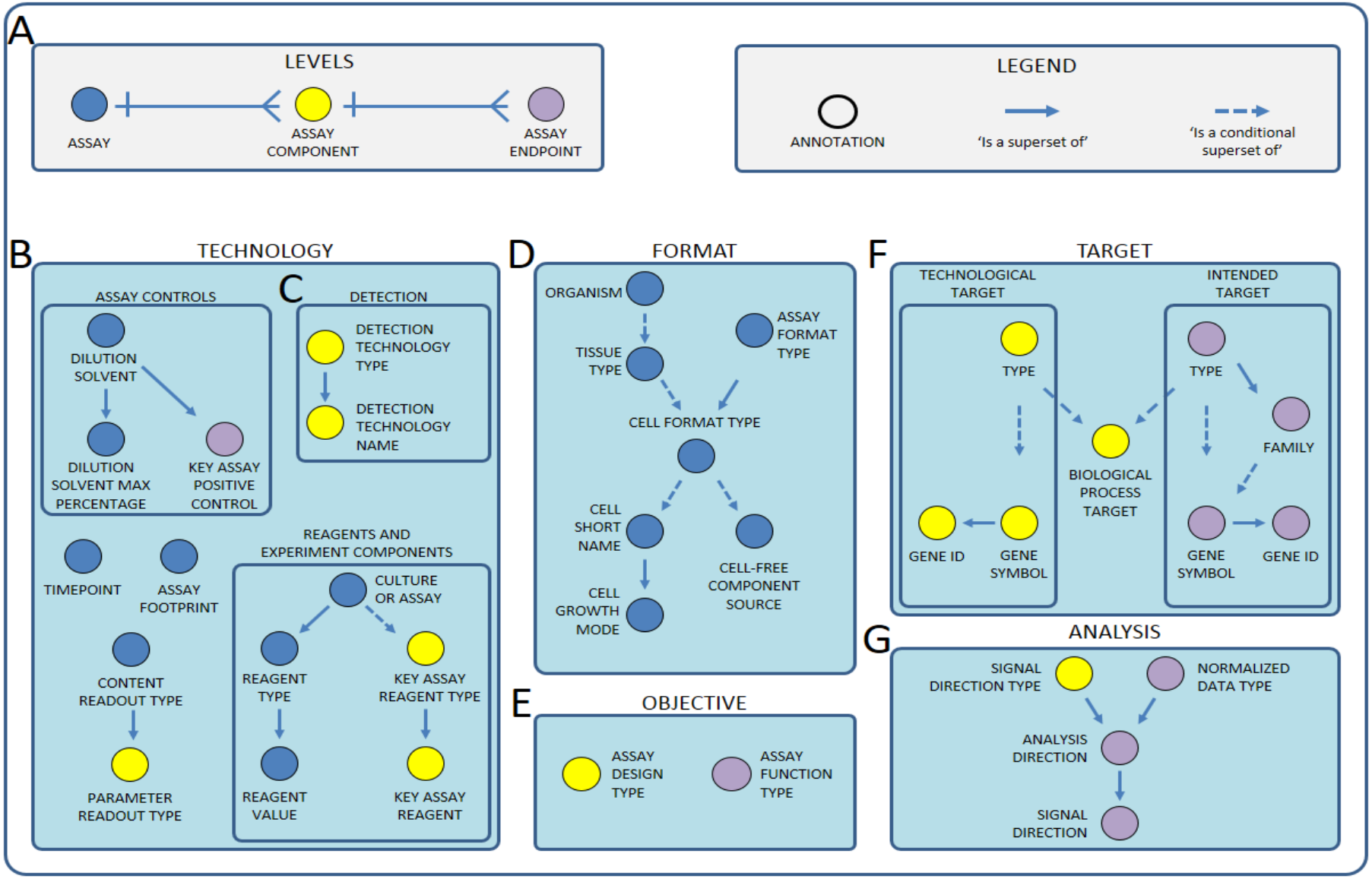
ToxCast Assay Annotation Objectives

- Provide the highest level of transparency
- Encourage confidence in assay activity
  - Need for a ***comprehensive description*** of in vitro assay methods to facilitate knowledgeable / accurate interpretation of results
  - Provide the elements necessary for accuracy in replication
- Provide detailed assay documentation to aid external evaluation
- Clearly define the nature of the response measured and its relevance for impacts on biological systems
  - ***Describe assay reliability*** (reproducibility), ***relevance*** (mechanistic modeling, downstream health effects, AOP applicability, etc.), ***and fitness-for-purpose*** (ability to predict outcomes similar to guideline studies)

Initial ToxCast Assay Annotation

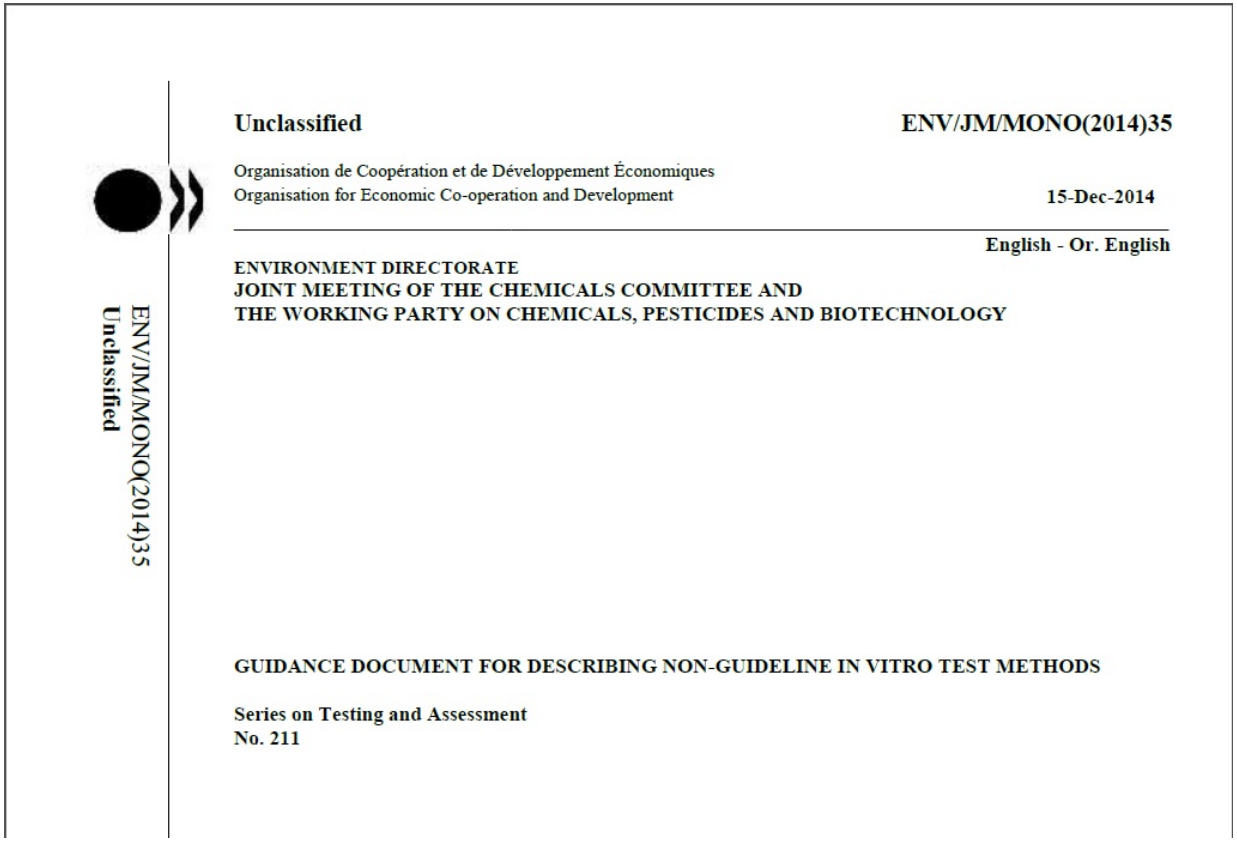
- Bioassay Ontology (BAO)-based *(Visser, U., et al. BMC Bioinformatics 12(1): 257, 2011.)*
- Formatted for computational analysis
- Need for more reader-friendly format
- Adapted OECD TG 211 Guidelines to fit ToxCast data structure

ToxCast Bioassay Ontology (BAO)-based Annotations



(Image from Phuong, J., *et al*. (2014). ToxCast Assay Annotation Version 1.0 Data User Guide. U.S. Environmental Protection Agency., pp. 36. https://www.epa.gov/sites/production/files/2015-08/documents/ toxcast_assay_annotation_data_users_guide_20141021.pdf).

Guidance for describing non-guideline in vitro test methods OECD Series on Testing and Assessment No. 211



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GUIDANCE DOCUMENT FOR DESCRIBING NON-GUIDELINE IN VITRO TEST METHODS

Series on Testing and Assessment
No. 211

- General information
- Test method definition
- Data interpretation and prediction model
- Test method performance
- Potential regulatory applications

ToxCast Assay Annotations

- ToxCast assays currently annotated using 45 different BAO-derived structured text descriptors arranged into hierarchical levels in multiple MySQL data tables:
  - **Assay** (exposure platform/summary information)

    May have multiple:

    - **Assay Component** (detection technology)

      May have multiple:

      - **Assay Component Endpoint** (technological readout)
- Easily searchable and readily amenable to bioinformatics approaches
  - May not provide the level of background context and detailed description desired for utility in chemical safety assessment considerations
- OECD template not directly transferable to *invitrodb* database architecture, but most required reporting elements available with slight re-arrangements of item order and sectioning

OECD Guidance Document № 211 Template:

1. General Information

- 1.1. Assay Name
- 1.2. Summary
- 1.3. Date of Method Description (MD)
- 1.4. MD author(s) and contact details
- 1.5. Date of MD update(s) and contacts
- 1.6. Assay developer(s)/laboratory and contact details
- 1.7. Date of assay development and/or publication
- 1.8. Reference(s) to main scientific paper
- 1.9. Availability of information about proprietary elements
- 1.10. Information about the throughput of the assay
- 1.11. Status of method development and uses
- 1.12. Abbreviations and Definitions

2. Test Method Definition

- 2.1. Purpose of the test method
- 2.2. Scientific principle of the method
- 2.3. Tissues, Cells or Extracts utilized in the assay
- 2.4. Metabolic competence of the test system
- 2.5. Description of the experimental system exposure regime
- 2.6. Response and response measurement
- 2.7. Quality / Acceptance criteria
- 2.8. Known technical limitations and strengths
- 2.9. Other related assays that characterize the same event as in Section 2.1

3. Data Interpretation and Prediction Models

- 3.1. Assay response captured by the prediction model
- 3.2. Data analysis
- 3.3. Explicit prediction model
- 3.4. Software name and version for algorithm/prediction model generation

4. Test Method Performance

- 4.1. Robustness of the method
- 4.2. Reference chemicals / chemical libraries, and rationale for selection
- 4.3. Performance measures / predictive capacity (where known)
- 4.4. Scope and limitations of the assay, if known

5. Potential Regulatory Use

6. Bibliography

7. Supporting Information

EPA NCCT ToxCast Assay Documentation Outline:

1. Assay Descriptions

Assay Overview (OECD № 211 outline equivalent)
- Assay Title (1.1)
- Assay Summary (1.2)

Assay Definition
- Assay Throughput (1.10)
- Experimental System (2.3)
- Xenobiotic Biotransformation Potential (2.4)
- Basic Procedure (2.5)
- Proprietary Elements (1.9)
- Caveats (2.8)

Assay References
- Assay Source Contact Information (1.6)
- Assay Publication Year (1.7)
- Assay Publication Citation (1.8)
- Method Updates / Confirmatory Studies (1.11)

2. Assay Component Descriptions
- Assay Objectives (2.1; 2.7; 4.2)
- Scientific Principles (2.2)
- Method Development References (2.2)

3. Assay Endpoint Descriptions

Data Interpretation
- Biological Response (2.6)
- Analytical Elements (3.2; 3.4; 4.3)
- Related ToxCast Assays (2.9)

Assay Performance
- Assay Quality Statistics (Robustness) (4.1)
- Assay Performance Measures (4.3)
- Reference Chemicals (4.2)
- Rationale For Selection Of Chemical Library (4.2; 4.4)

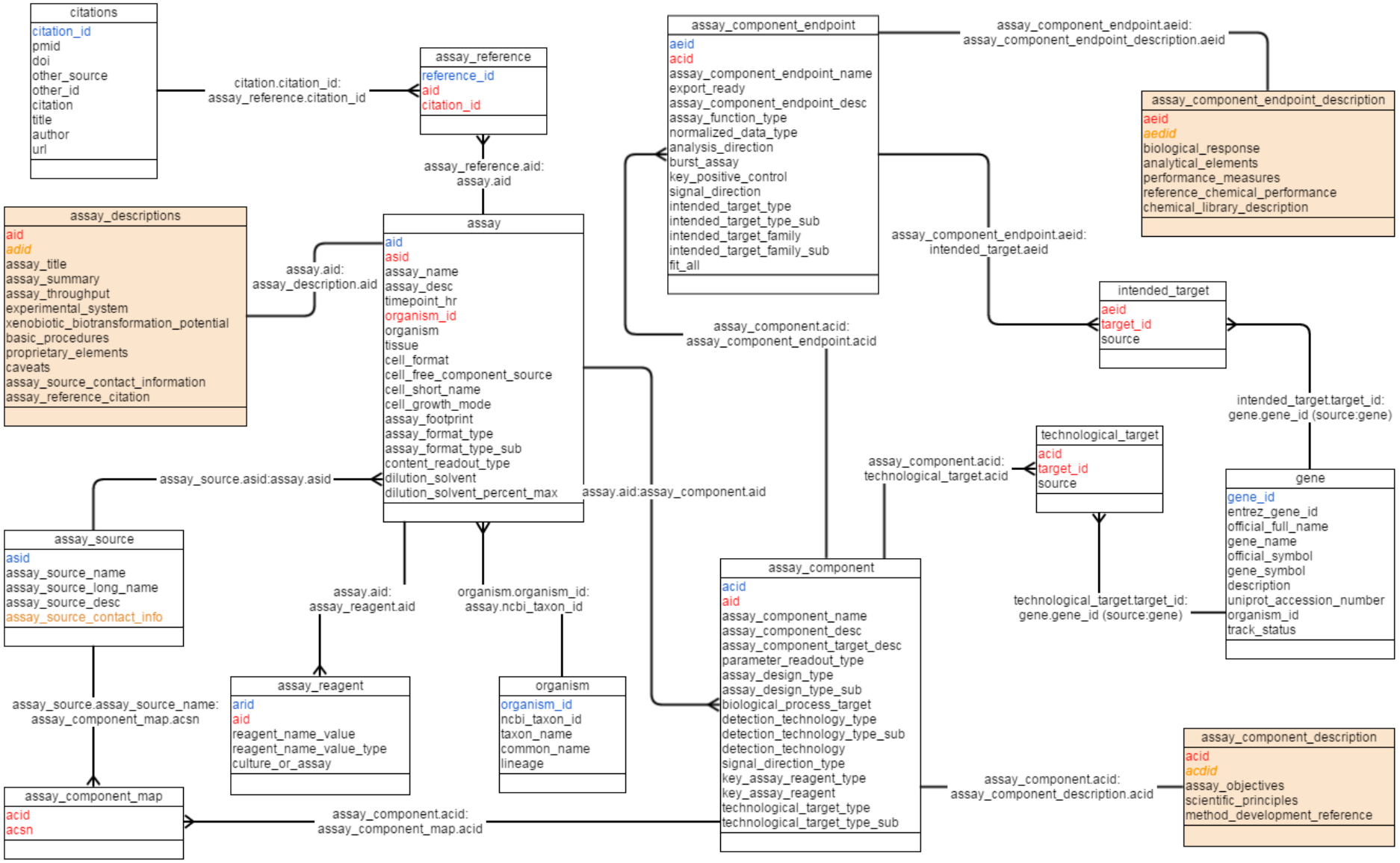
4. Assay Documentation

Assay Documentation Definition
- References (Section 6)
- Definitions / Abbreviations (1.12)

Assay Documentation Source
- Contact Information (1.4)
- Date of Assay Document Creation (1.3)
- Date/ Author of Revisions (1.5)

5. Supporting Information
- Existing ToxCast Annotations (Section 7)

ToxCast Assay Description Document Database;
Integration into *invitrodb*



Summary

- New ToxCast assay annotation covers virtually all of OECD Guidance Document No. 211
- Organization of documents differs due to underlying differences in ToxCast data structure
- Some redundancy in different OECD descriptions streamlined for accelerated production of documentation;
  - *e.g.,* "Potential Regulatory Application" section merged into "Assay Objectives" description item
- Summary (assay-level) descriptions planned to be made available through PubChem BioAssay
- Endocrine-relevant assay descriptions ready to be made available in CompTox Dashboards with next update
- Suggestions welcome
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